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The Toronto Adolescent and Youth Cohort Study: Study Design and Early Data Related to Psychosis Spectrum Symptoms, Functioning, and Suicidality

Kristin Cleverley, George Foussias, Stephanie H. Ameis, Darren B. Courtney, Benjamin I. Goldstein, Lisa D. Hawke, Nicole Kozloff, Lena C. Quilty, Martin Rotenberg, Anne L. Wheeler, Brendan F. Andrade, Madison Aitken, Don Mahleka, Melanie Jani, Margot Frayne, Jimmy K.Y. Wong, Rachel Kelly, Erin W. Dickie, Daniel Felsky, John D. Haltigan, Meng-Chuan Lai, Yuliya S. Nikolova, Wanda Tempelaar, Wei Wang, Marco Battaglia, Muhammad Omair Husain, Sean Kidd, Paul Kurdyak, Robert D. Levitan, Stephen P. Lewis, Alexia Polillo, Peter Szatmari, Anna I.R. van der Miesen, Masoud Ahmadzadasl, Aristotle N. Voineskos, and the TAY Cohort Study Team

ABSTRACT

BACKGROUND: Psychosis spectrum symptoms (PSSs) occur in a sizable percentage of youth and are associated with poorer cognitive performance, poorer functioning, and suicidality (i.e., suicidal thoughts and behaviors). PSSs may occur more frequently in youths already experiencing another mental illness, but the antecedents are not well known. The Toronto Adolescent and Youth (TAY) Cohort Study aims to characterize developmental trajectories in youths with mental illness and understand associations with PSSs, functioning, and suicidality.

METHODS: The TAY Cohort Study is a longitudinal cohort study that aims to assess 1500 youths (age 11–24 years) presenting to tertiary care. In this article, we describe the extensive diagnostic and clinical characterization of psychopathology, substance use, functioning, suicidality, and health service utilization in these youths, with follow-up every 6 months over 5 years, including early baseline data.

RESULTS: A total of 417 participants were enrolled between May 4, 2021, and February 2, 2023. Participants met diagnostic criteria for an average of 3.5 psychiatric diagnoses, most frequently anxiety and depressive disorders. Forty-nine percent of participants met a pre-established threshold for PSSs and exhibited higher rates of functional impairment, internalizing and externalizing symptoms, and suicidality than participants without PSSs.

CONCLUSIONS: Initial findings from the TAY Cohort Study demonstrate the feasibility of extensive clinical phenotyping in youths who are seeking help for mental health problems. PSS prevalence is much higher than in community-based studies. Our early data support the critical need to better understand longitudinal trajectories of clinical youth cohorts in relation to psychosis risk, functioning, and suicidality.

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Among psychiatric syndromes, psychosis is especially disabling and is associated with cognitive impairment, long-term disability, and death by suicide (1). The major psychoses, schizophrenia and bipolar I disorder, are collectively among the leading causes of disability (2). However, the presence of psychotic symptoms in nonpsychotic disorders is also disproportionately associated with significant negative consequences. For example, people with psychotic depression experience a more severe course of illness, have more hospitalizations, and are more likely to die by suicide than individuals with nonpsychotic depression (3). Neurodevelopmental traits and disorders, such as autism spectrum disorder (ASD), are associated with psychotic experiences (PEs) (4), which in turn are associated with poorer functioning and more severe suicidality (i.e., suicidal thoughts and behaviors) (5). The adverse impact of PEs appears to be highest in youths (6).

Considerable investment in the early identification of psychosis has occurred via the clinical high risk (CHR) or prodromal psychosis syndrome (7). However, only a small percentage of individuals who develop a psychotic disorder (~5%) are identified by CHR criteria, typically using community-based sampling strategies (8). Therefore, alternative strategies are needed to identify the majority of youths

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who develop psychosis, as well as the impact of psychosis spectrum symptoms (PSSs) in youths who do not develop a psychotic disorder. Such strategies complement current CHR research and may identify additional youths with CHR and allow for novel opportunities for early identification and prevention.

Major population-based cohort studies have helped highlight the prevalence, functional impact, and neurobiological underpinnings of PSSs and psychotic-like experiences in children and youths. Catchment area studies, such as the Philadelphia Neurodevelopmental Cohort (PNC) (9) and the U.S.-wide Adolescent Brain Cognitive Development (ABCD) Study (10) are notable examples. In the PNC, the presence of any diagnosed childhood psychiatric disorder increased the likelihood of a PSS designation compared with youths without a psychiatric disorder (9). The Avon Longitudinal Study of Parents and Children birth cohort also showed that any childhood disorder at age 8 predicted PEs at age 13 (11). The ABCD Study, which aims to follow almost 12,000 children in the general population from 9 to 10 years of age for a 10-year period (12), revealed significant relationships of psychotic-like experiences with internalizing symptoms and, to a lesser extent, externalizing symptoms in 3984 participants (13). Thus, all of the PEs, psychotic-like experiences, and PSSs are more common in children and youths already experiencing other mental health symptoms.

Other notable large-scale initiatives that have examined developmental psychopathology in youths include the Healthy Brain Network (HBN) (14), a multimodal investigation of a heterogeneous community-referred sample of youths and families; the IMAGEN study (15), a longitudinal imaging-genetics community-based study investigating risk of psychiatric disorders in a cohort of 14-year-old youths; and the High Risk Cohort Study for the Development of Childhood Psychiatric Disorders (16), a school-based study investigating developmental trajectories of psychopathology and psychiatric disorders in a cohort of children and youths. While complementary in their developmental psychopathology focus, these studies have not been focused specifically on early impacts of PSSs in youths.

Health administrative data have revealed that most youths who develop a first episode of psychosis have already presented for mental health care. Nearly 75% of people with a first episode of psychosis have already had contact for a mental health concern during the 3 years prior to their first presentation for psychosis (17). Registry and catchment-area study data suggest that a diagnosis of a childhood disorder, such as ASD, disruptive behavior disorder, or a mood or anxiety disorder early in life, is each associated with an elevated risk of developing psychosis (11,18). Therefore, children and youth at risk for psychosis may be hiding in plain sight in mental health services conventionally geared toward young people with nonpsychotic disorders. It is unclear whether the presence of PSSs adds predictive value beyond the presence of a childhood disorder in predicting psychosis.

The Toronto Adolescent and Youth (TAY) Cohort Study aims to prospectively characterize the developmental trajectories of PSSs, functioning, and suicidality in youths who are seeking help for mental health problems and identify their outcomes and antecedents. The TAY Cohort Study fills the gap between large general population cohort studies that have shown the adverse impact of PEs/psychotic-like experiences/PSSs and retrospective health administrative data showing that most youths with a first psychotic episode had previously sought mental health care. For study participants receiving care in hospital-based clinics, the electronic health record and linkage to health administrative data in a single-payer system provide unique opportunities for primary data collection and in terms of retention. In companion papers on this issue, the detailed cognitive and educational achievement (19) and imaging and biosample assessments (20) that are a part of the protocol are described. Here, we describe the aspects of the study related to demographics, mental health, physical health, service utilization, and functioning. We also describe baseline characteristics of the first 417 participants recruited between May 4, 2021, and February 2, 2023.

The primary aims for the mental and physical health and service use data in the TAY Cohort Study are to 1) establish the developmental trajectories of PSSs and their relationship to trajectories of functioning and risk for suicide attempts across a 5-year period; 2) characterize the dimensional and categorical antecedents/predictors of longitudinal PSS trajectories and how these are related to cognitive, familial, social, and environmental factors; and 3) identify the relationship between PSSs and retrospective and current patterns of prior health service use in youths seeking mental health treatment and emerging adults (youth) with mental illness.

An exploratory aim of the study is to determine early PSS and functioning signatures (i.e., across the first 1–2 years) that are predictive of trajectories overall (across 5 years) and of a first psychotic episode.

The detailed aims and hypotheses are described in the Supplement.

METHODS AND MATERIALS

Study Design Overview

The TAY Cohort Study aims to recruit youths seeking mental health and/or substance use services at the Centre for Addiction and Mental Health (CAMH), in Toronto, Ontario, Canada, a large tertiary care psychiatric hospital, with a 5-year follow-up period of prospective data collection. Assessments evaluate mental health symptoms, physical health, social and health equity, and health service utilization, which are described below, along with cognitive and education attainment and biological samples and imaging, which are described by Quilty *et al.* (19) and Dickie *et al.* (20), respectively. An overview of the TAY Cohort Study is shown in Figure 1. The TAY study aims to recruit and characterize 1500 youths longitudinally across all data types, i.e., mental/physical health, service use, cognitive/educational, and biological data.

Participants

Eligible youth participants are those who are 11 to 24 years old and currently seeking and/or accessing mental health services at CAMH. Participants are excluded if they do not provide informed consent (for those with the capacity to consent) or assent (for those who lack the capacity to consent) or if they are nonverbal and/or do not speak English. We do not actively

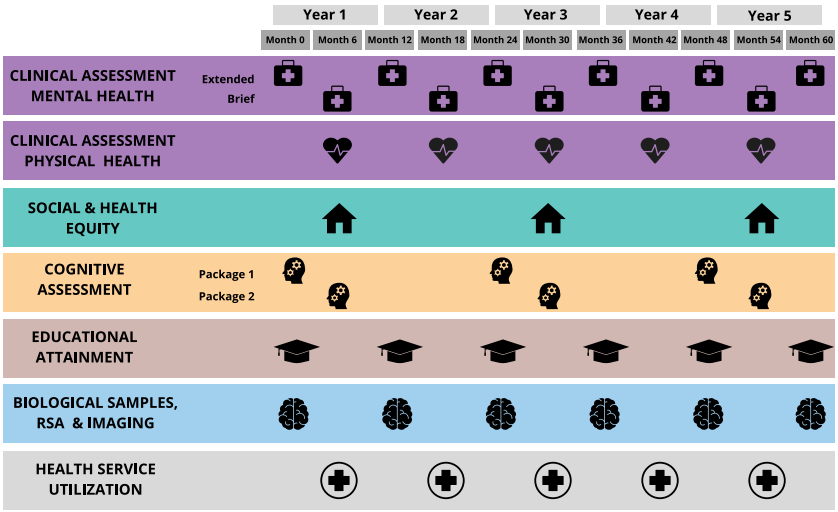

Figure 1. Overview of the Toronto Adolescent and Youth Cohort Study assessment schedule. Clinical assessments of mental health, physical health, social and health equity, and health service utilization are described in this article. Cognitive and educational attainment assessments have been described by Quilty *et al.* (19), and biological samples and imaging have been described by Dickie *et al.* (20). RSA, respiratory sinus arrhythmia.

recruit youths with a primary psychotic disorder at baseline given that psychosis is a potential outcome of interest. For those who lack the capacity to consent, the inability of the legal guardian to provide informed consent for the youth is also an exclusion criterion. This study was approved by the CAMH Research Ethics Board and complies with the World Medical Association Declaration of Helsinki (21).

All child and youth services across CAMH serving youths in the 11- to 24-year age range are engaged in the recruitment process. A multimethod approach for participant recruitment is utilized, with strategies developed and monitored in partnership with youth and caregiver advisers to enhance participant and caregiver experiences (22). All youth participants provide written informed consent or assent combined with written informed consent from their substitute decision maker for those youths who do not have the capacity to consent. Each youth participant is invited to involve a caregiver (e.g., parent, sibling) in the study. If a youth consents to their caregiver's participation, the caregiver's information is provided to a research staff member, who then reviews the consent form with the caregiver, and informed consent is documented. Caregiver participants must be able to communicate in English and provide written informed consent to participate.

Measures

Clinical Assessments at Baseline (Repeated Annually). All youth participants are characterized with clinical assessments (Table 1) at baseline and during longitudinal follow-up. Measures were selected based on their relevance to the research aims with a focus on dimensional measures, favorable psychometric properties, feasibility for use in a large sample, and harmonization across existing projects, including the ABCD Study (10) and PNC (9) studies. Given the high prevalence of mental health multimorbidity in youths with mental illness and the objective of understanding antecedents and risk for PSSs and psychotic disorders, we ensured categorical and dimensional coverage of major groups of DSM-5–defined disorders. Youths and caregivers with lived experience were engaged to help select measures and guide assessment delivery (see the Supplement for additional information related to youth, caregiver, and clinical engagement).

The revised PhenX Toolkit Demographic Protocol (23), updated and adapted based on youth and caregiver feedback, is administered to all participants to ascertain key demographic information including family composition, parent occupation and income, sex assigned at birth, current gender identity, race and ethnicity, and immigration history. To determine the presence of categorical mental health diagnoses, participants between 11 and 17 years of age and their caregiver are administered the Kiddie Schedule for Affective Disorders and Schizophrenia - Present and Lifetime (24), with the Structured Clinical Interview for DSM-5 (25) used for youths 18 years and older. Functioning and disability are assessed in all youth participants through the Columbia Impairment Scale (self-report) (26,27) to measure impairment in major areas of functioning, the World Health Organization Disability Assessment Schedule 2.0 (self-report version) to assess overall health and disability (28), and the Global Functioning Social and Role scales to measure social and role functioning (29).

For the evaluation of PSSs, all youth participants were administered the PRIME Screen–Revised (30), as well as the Prodromal Questionnaire–Brief (31) and the Scale of Prodromal Symptoms–Negative/Disorganized subscales (32). Dimensional psychopathology is evaluated using the Achenbach measures: the Youth Self-Report (YSR) for youths 11 to 17 years of age and the Adult Self-Report (ASR) for youths 18 years and over (33). The Social Responsiveness Scale–Short Form (34), with the self-report form for youths 18 years and over (in addition to caregiver report detailed below) is used to capture reciprocal social behavior/social impairment. The Columbia-Suicide Severity Rating Scale (35) is administered to all youth participants to measure lifetime and past-year suicidal ideation, suicidal behavior, and nonsuicidal self-injury (NSSI). As per the Columbia-Suicide Severity Rating Scale, suicidal behaviors include actual suicide attempts, interrupted

Table 1. Toronto Adolescent and Youth Cohort Study Schedule of Assessments—Clinical Assessments of Mental Health, Physical Health, Social and Health Equity, and Service Utilization

Measure	Age Range, Years	Informant	Time Point, Months									
			0	6	12	18	24	30	36	42	48	54	60
Personal Information													
Personal information form	All	RA/SR	X										
Additional contact information form	All	RA/SR	X										
Diagnostic													
The Kiddie Schedule for Affective Disorders and Schizophrenia for DSM-5	11–17	RA	X				X				X		
The Structured Clinical Interview for DSM-5	18+	RA	X				X				X		
Psychosis													
PRIME Screen–Revised	All	SR	X	X			X		X		X		X
Prodromal Questionnaire–Brief	All	SR	X	X			X		X		X		X
Scale of Prodromal Symptoms–Negative/disorganized Subscales	All	RA	X	X			X		X		X		X
General Psychopathology													
Youth self-report	11–17	SR	X	X			X		X		X		X
Adult self-report	18+	SR	X	X			X		X		X		X
Child Behavior Checklist	11–17	CG	X	X			X		X		X		X
Autism Spectrum													
Social Responsiveness Scale–Short Form	SR: 18+ Ca: all	SR/CG	X	X			X		X		X		X
Social Communication Questionnaire	All	CG		X									
Suicidal Ideation and Behaviors and Nonsuicidal Self-Injury													
Columbia-Suicide Severity Rating Scale	All	RA	X	X			X		X		X		X
Self-Injurious Thoughts and Behaviors Interview–Nonsuicidal Self-Injury	All	RA	X	X			X		X		X		X
Suicidal Ideation Questionnaire–Junior	All	SR	X	X			X		X		X		X
Substance Use													
The Adolescent Alcohol and Drug Involvement Scale–Revised/grid	All	SR	X	X			X		X		X		X
Functioning													
Columbia Impairment Scale (Self- and Caregiver Report)	All	SR/CG	X	X			X		X		X		X
Global Functioning: Social and Role Scales	All	RA	X	X			X		X		X		X
The Self-Report World Health Organization – Disability Assessment Schedule-12 Item (2.0–Self and Proxy Versions)	All	SR/CG	X	X			X		X		X		X
Health Service Utilization													
Health and social service utilization	All	SR		X		X		X		X		X	
Adolescent health history	All	SR/CG		X				X				X	
Personality Psychopathology													
Personality Inventory for DSM-5-Faceted Brief Form	All	SR		X		X		X		X		X	
Physical Health													
Developmental History Questionnaire	All	CG		X				X				X	
Medication inventory	All	SR/CG		X				X				X	
Modified Ohio State University Traumatic Brain Injury Screen–Short Version	All	SR		X				X				X	
Puberty Scale	All	SR		X				X				X	
International Physical Activity Questionnaire	All	SR		X				X				X	
Height, weight, body mass index, waist circumference, and blood pressure	All	RA		X				X				X	
Pain questionnaire	All	SR		X				X				X	
Pittsburgh Sleep Quality Index	All	SR		X				X				X	
Risky Behavior: Things I Do Questionnaire	All	SR		X				X				X	
Social and Health Equity													
PhenX Toolkit Demographic Protocol	All	SR/CG	X				X				X		
Vancouver Index of Acculturation–Short	All	SR/CG		X				X				X	
Multigroup Ethnic Identity - Revised	All	SR/CG		X				X				X	
PhenX Toolkit Acculturation Questionnaire	All	SR/CG		X				X				X	
Mexican American Cultural Values Scale	All	SR		X				X				X	
Gender Identity/Gender Dysphoria Questionnaire for Adolescents and Adults	All	SR		X				X				X	

Table 1. Continued

Measure	Age Range, Years	Informant	Time Point, Months 0	6	12	18	24	30	36	42	48	54	60
Personal Attributes Questionnaire	All	SR	X					X				X	
Everyday Discrimination Scale	All	SR	X					X				X	
Adverse Life Events Scale	12–17	SR/CG	X					X				X	
Life Events Checklist	18+	SR	X					X				X	
Childhood Trauma Questionnaire–Short Form	All	SR	X					X				X	
Connor-Davidson Resilience Scale–2-Item	All	SR	X					X				X	
Attachment Script Assessment–Adolescent Version	All	RA	X					X				X	
Prosocial Scale From the Strengths and Difficulties Questionnaire–Prosocial Subscale	All	SR/CG	X					X				X	
Parental Monitoring Survey	All	SR	X					X				X	
Conflict Behavior Questionnaire	All	SR/CG	X					X				X	
PhenX Toolkit Neighbourhood Safety and Crime Scale	All	SR/CG	X					X				X	
PhenX Toolkit Inventory for School Risk & Protective Factors Survey	12–18	SR	X					X				X	

Measures are referenced in the Methods and Materials and in the Supplement. Cognitive and educational attainment assessments have been described by Quilty *et al.* (19), and biological samples and imaging have been described by Dickie *et al.* (20).

CG, caregiver report; RA, rater-administered; SR, youth self-report.

attempts, aborted attempts, preparatory behaviors, and death by suicide. If a participant reports NSSI on the single item for NSSI on the Columbia-Suicide Severity Rating Scale, they are also administered the relevant subsection of the Self-Injurious Thoughts and Behaviors Interview (36) to further evaluate NSSI. In addition, self-reported suicidal ideation in the past 30 days is assessed using the Suicidal Ideation Questionnaire–Junior (37). To quantify the frequency of past-year substance use, youth participants complete the self-report Adolescent Alcohol and Drug Involvement Scale–Revised/Grid (38).

Clinical Assessments—Caregiver Report (Baseline and Repeated Annually). In addition to youth-administered measures, caregiver participants complete the Columbia Impairment Scale caregiver-report version (26,27) and the World Health Organization Disability Assessment Schedule 2.0 proxy version (28) to provide complementary evaluation of youth participant functioning. Caregiver participants are also administered the Child Behavior Checklist caregiver-report version for youth participants 11 to 17 years of age (33), the Social Responsiveness Scale–Short Form caregiver-report form for all youth participants (34), as well as the caregiver-report Social Communication Questionnaire to measure current and developmental cardinal autism symptoms (39).

Clinical Assessments—Mental Health Brief (Months 6, 18, 30, 42, and 54) and Physical Health (Months 6, 30, and 54). To address the assessment burden at 0, 12, 24, 36, 48, and 60 months, and to enhance retention, additional mental health and physical health assessments are conducted at the 6-month "off" intervals. These are detailed in the Supplement, as are social and health equity assessments.

Health Administrative and Health System Utilization Data Collection

Linked health and other administrative data for the population of Ontario are overseen by the Institute for Clinical Evaluative Sciences, which allows for analysis of utilization and cost of most publicly funded services. Youth participants are asked to consent to linkage of their primary study data with data held at the Institute for Clinical Evaluative Sciences. Data will be examined from birth or when the participant first became eligible for Ontario Health Insurance Plan coverage (e.g., if they moved to Ontario), and observation for outcomes of interest will continue until they move out of the province and lose coverage or until the time of their death. This provides the unique opportunity to examine long-term outcomes of interest, including diagnosis of a psychotic disorder, presentations to the emergency department for self-harm, and mortality. In addition, more detailed mental health, physical health, and social service utilization will be obtained via self-report using a locally adapted version of the Health and Social Service Utilization measure (40–42) with additional items from the Ontario Student Drug Use and Health Survey (43–45).

Statistical Analyses

For the baseline cross-sectional characterization that is the focus of the analysis of data from the early youth participants presented below, descriptive statistics were calculated across demographic, clinical, and community functioning measures. Youth participants were categorized as PSS or non-PSS using the Extreme Agreement Index on the PRIME Screen–Revised (≥1 item rated 6 "definitely agree" or ≥3 items rated 5 "somewhat agree"), similar to the method described by Calkins *et al.* (9). Comparisons between PSS and non-PSS participants were conducted using nonparametric Mann-Whitney *U* tests for continuous variables and Fisher's exact tests with 100,000 random permutations for categorical variables, as appropriate, to evaluate differences in demographic variables, clinical symptoms, and community functioning between groups. Effect size was evaluated using Cohen's *d* and Cohen's ω for continuous and categorical variables, respectively.

For the longitudinal aims of the TAY Cohort Study, latent growth curve and growth mixture modeling were applied to characterize developmental trajectories of PSSs and functioning (aim 1). Growth mixture modeling provides a versatile

framework to examine whether hypothesized covariates, including cognitive, familial, social, and environmental factors differ in prevalence or degree across distinct classes of growth trajectories (aim 2). Similar approaches were applied to examine the association between PSSs and retrospective and current patterns of health service use (aim 3). Generalized linear models were used to associate previous service use with PSSs, and parallel processes and cross-lagged models were used to associate current service use and PSSs concurrently. For the exploratory aim, the youth's early performance on PSSs and functioning were associated with the overall growth trajectory classes across 5 years using generalized linear modeling, with the latter treated as a categorical outcome.

Additional details regarding computations of total scores across all measures, the longitudinal statistical analysis plan, and sample size considerations are described in the Supplement. All analyses were conducted using SAS, R, and Mplus software packages.

RESULTS

Participant Characteristics

Between May 4, 2021, and February 2, 2023, 657 youth participants were screened, 436 consented to participate, and 436 were eligible and enrolled in the study. Among enrolled participants, 417 youth participants were included in the analysis who met the following criteria: 1) completed any baseline assessments before February 2, 2023 (n = 393) or 2) withdrew from the study or was lost to follow-up before completing any assessments (n = 24). Among those 417 participants, 86.6% completed all baseline study assessments, and 42.9% (n = 179) of youth participants also had caregiver participation. In addition, 93.8% of youth participants consented to linkage of their study data with administrative health data through the Institute for Clinical Evaluative Sciences.

This early sample of youth participants had a mean age of 18.4 years (SD 3.73), 63% were assigned female at birth, and 67% identified as cisgender girls/women or cisgender boys/men. In terms of categorical diagnoses, participants met criteria for an average of 3.5 categorical mental disorder domains (Figure 2). The most frequent categorical diagnoses were anxiety disorders (80.3%) and depressive disorders (73.2%). Neurodevelopmental disorders, comprised of attention-deficit/hyperactivity disorder, tic disorders, and ASD, were the third most common (51.7%).

PSS Prevalence and Relationships with Demographic and Clinical Characteristics and Community Functioning

Across participants who had completed the PRIME Screen–Revised (n = 374), 49.2% (n = 184) met criteria for PSSs. Demographic and clinical characteristics of this sample who completed the PRIME Screen–Revised are shown in Tables 2 and 3. There were no significant differences in demographic characteristics between youth participants who had completed the PRIME Screen–Revised and those who did not (n = 43).

Evaluation of dimensional psychopathology with the YSR and ASR revealed high prevalence of clinically significant psychopathology across syndromes (i.e., a YSR or ASR syndrome scale T score ≥70)—anxious/depressed syndrome (39.6%), withdrawn/depressed syndrome (23.8%), somatic complaints syndrome (19.8%), thought problems (26.2%), attention problems (31.6%), rule-breaking behavior (13.9%), aggressive behavior (11.8%), and social problems for those administered the YSR (20.6%). These youth participants also reported high rates of suicidality in the past year, with 19.8% reporting suicidal behavior, 10.4% reporting a suicide attempt(s), and 35.8% reporting NSSI.

The PSS group exhibited significantly higher functional impairment than the non-PSS group as measured by the Columbia Impairment Scale, the World Health Organization Disability Assessment Schedule 2.0, and the Global Functioning Social and Role scales, with moderate to large effect sizes across all measures except Social Functioning, which demonstrated a small effect size (Table 3). The PSS group also demonstrated significant elevations across psychopathology syndromes (via the YSR/ASR) with moderate to large effect sizes, negative and disorganized symptoms (via the Scale of Prodromal Symptoms) of moderate effect size, and significantly elevated scores on the Social Responsiveness Scale–Short Form with moderate effect size. The PSS group also exhibited significantly higher rates of current suicidality than the non-PSS group, including elevated suicidal ideation and NSSI, as well as suicidal behavior and attempts. Alcohol and drug involvement were not different between the PSS and non-PSS groups.

DISCUSSION

The TAY Cohort Study aims to characterize the antecedents and developmental trajectories of PSSs and the impact of these symptoms on trajectories of functioning and suicidality in youths seeking mental health services. Initial findings from the first 417 participants demonstrate the feasibility of extensive clinical phenotyping in this population. We found very high rates of completion of study assessments across a diverse sample (e.g., in terms of sex assigned at birth and gender identity) and age range of youth participants, with 86% completing all baseline assessments. Furthermore, more than 90% of participants agreed to linkage to provincial health administrative data that includes health service utilization data across a single-payer publicly funded healthcare system.

Initial results from the TAY Cohort Study reveal high PSS prevalence in youths presenting for mental health services for reasons not related to a psychotic disorder. The elevated prevalence of PSS in this help-seeking sample (~49%) is much higher than that identified in previous community cohort studies (~10–20%) (9,46), although consistent with other studies that have examined children and adolescents accessing mental health services (46–48). The adverse impact of PSSs on youths is similar across domains (9,46,47). PSSs were associated with greater functional impairment across a range of measures of functioning and disability, substantially elevated rates of both internalizing and externalizing psychopathology, and suicidality.

There was notably higher gender diversity in youths who met PSS criteria than in the non-PSS group. This initial observation echoes the limited research conducted to date on psychosis risk in gender-diverse populations (49). Our

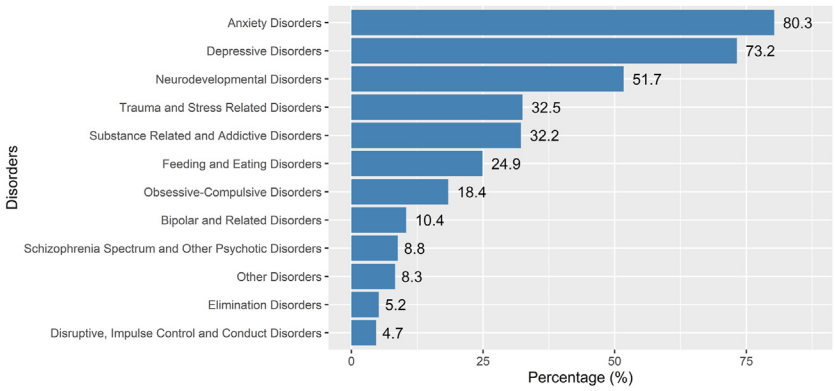

Figure 2. Prevalence of DSM-5 disorders in youth participants. The percentages of youth participants who met criteria for DSM-5 categorical diagnoses are shown. Diagnoses are grouped in high-level DSM-5 categories, with neurodevelopmental disorders encompassing attention-deficit/hyperactivity disorder, tic disorders, and autism spectrum disorder, and other disorders including other unspecified mood and other unspecified mental disorders.

longitudinal design affords an opportunity to examine relationships among gender diversity, socioenvironmental factors, and psychosis risk trajectories.

Our findings also reveal extensive mental health multimorbidity in this population, where almost 50% exhibit threshold PSSs and simultaneously have an average of 3.5 categorical DSM diagnoses. Through the TAY Cohort Study, we will have an opportunity to evaluate the evolution of categorical diagnoses and how this tracks with trajectories of PSS and functioning, as well as with trajectories at highest risk for the development of a psychotic disorder. This also represents a unique opportunity to evaluate both categorical and dimensional contributors to trajectories and outcomes in a broad and representative sample of youths accessing mental health services.

Early identification of PSSs, and in particular the subgroup of individuals who experience persistence of emerging PSS trajectories during this early developmental stage in life, enables opportunities to advance efforts at early intervention. Previous findings have highlighted that a subgroup of individuals with PSSs continue to exhibit either persistent PSSs over a 12-month period, or emergent PSSs over time, although others exhibit resolution of PSS over this same period of time (50). Similarly, findings in youths at CHR for psychosis indicate that not all youths who experience PSSs will go on to develop a primary psychotic disorder (51). Identification of those youths who are at the highest risk of developing a psychotic disorder is essential to enable targeted intervention (52).

Table 2. Demographic Characteristics of Participants With and Without Psychosis Spectrum Symptoms

Demographic Variable	All, *n* = 374	PSS, *n* = 184	Non-PSS, *n* = 190	*p* Value
Age at Enrollment, Years	18.3 (3.75)	18.2 (3.56)	18.3 (3.94)	.738
Sex Assigned at Birth				.0312
Female	252 (67.4%)	131 (71.2%)	121 (63.7%)	
Intersex	0 (0%)	0 (0%)	0 (0%)	
Male	119 (31.8%)	50 (27.2%)	69 (36.3%)	
Prefer not to answer	3 (0.8%)	3 (1.6%)	0 (0%)	
Gender Identity				.0339
Boy/man	112 (30.1%)	50 (27.3%)	62 (32.8%)	
Gender nonbinary/another gender identity	90 (24.2%)	55 (30.1%)	35 (18.5%)	
Girl/woman	170 (45.7%)	78 (42.6%)	92 (48.7%)	
Transgender or Gender Diverse				<.001
No	267 (71.8%)	116 (63.4%)	151 (79.9%)	
Yes	105 (28.2%)	67 (36.6%)	38 (20.1%)	
Ethnicity/Race				.0414
Another ethnicity	29 (7.8%)	18 (9.8%)	11 (5.8%)	
Black	17 (4.5%)	12 (6.5%)	5 (2.6%)	
East Asian	15 (4.0%)	5 (2.7%)	10 (5.3%)	
Mixed	84 (22.5%)	48 (26.1%)	36 (18.9%)	
Southeast Asian	19 (5.1%)	10 (5.4%)	9 (4.7%)	
White	210 (56.1%)	91 (49.5%)	119 (62.6%)	

Data are presented as *n* (%), except age at enrollment, which is shown in mean (SD) format. Statistical test results shown are for comparisons of the PSS and non-PSS groups.

PSS, psychosis spectrum symptom.

Table 3. Clinical Symptoms and Community Functioning of Participants With and Without Psychosis Spectrum Symptoms

Measure	All, *n* = 374	PSS, *n* = 184	Non-PSS, *n* = 190	*p* Value	Effect Size[a]
CIS SR Total Score	19.4 (9.86)	22.5 (10.0)	16.6 (8.80)	<.001	0.63
WHODAS SR Total Score	25.9 (8.69)	29.0 (9.02)	22.9 (7.25)	<.001	0.74
GF–Social Total Score	7.37 (1.48)	7.22 (1.52)	7.52 (1.44)	.017	0.21
GF–Role Total Score	6.85 (2.26)	6.30 (2.49)	7.38 (1.88)	<.001	0.49
PRIME Screen–Revised Total Score	25.6 (18.8)	39.9 (14.2)	11.8 (10.6)	<.001	2.25
PQ-B Total Sum Score	7.99 (5.39)	11.5 (4.87)	4.59 (3.28)	<.001	1.67
PQ-B Total Distress Score	26.5 (21.3)	40.3 (20.8)	13.2 (10.7)	<.001	1.65
SOPS Negative Subscale Score	1.31 (1.03)	1.57 (1.01)	1.05 (0.99)	<.001	0.52
SOPS Disorganized Subscale Score	0.77 (0.70)	0.99 (0.75)	0.56 (0.58)	<.001	0.65
C-SSRS: Suicide Ideation Severity (Past Year)	1.92 (1.76)	2.41 (1.80)	1.46 (1.58)	<.001	0.57
C-SSRS: Any Suicidal Behavior (Past Year)[b]	74 (19.8%)	49 (26.6%)	25 (13.2%)	.001	0.18
C-SSRS: Suicide Attempt (Past Year)[b]	39 (10.4%)	29 (15.8%)	10 (5.3%)	<.001	0.18
Any NSSI (Past Year)[b]	134 (35.8%)	83 (45.1%)	51 (26.8%)	<.001	0.2
SIQ-Jr. Total Score	24.0 (21.4)	33.2 (23.1)	14.5 (14.4)	<.001	0.97
YSR/ASR: Anxious/Depressed Syndrome Scale	68.3 (13.1)	72.6 (12.7)	64.3 (12.2)	<.001	0.68
YSR/ASR: Withdrawn/Depressed Syndrome Scale	63.6 (10.6)	66.2 (11.3)	61.1 (9.4)	<.001	0.49
YSR/ASR: Somatic Complaints Syndrome Scale	62.0 (10.3)	65.8 (11.1)	58.4 (7.8)	<.001	0.78
YSR/ASR: Thought Problems Syndrome Scale	64.6 (10.6)	70.2 (10.6)	59.3 (7.3)	<.001	1.2
YSR/ASR: Attention Problems Syndrome Scale	66.2 (11.7)	69.9 (11.8)	62.8 (10.4)	<.001	0.64
YSR/ASR: Rule-Breaking Behavior Syndrome Scale	60.2 (9.8)	63.4 (10.6)	57.2 (7.9)	<.001	0.66
YSR/ASR: Aggressive Behavior Syndrome Scale	59.5 (9.3)	62.9 (10.4)	56.3 (6.8)	<.001	0.76
YSR: Social Problems Syndrome Scale[c]	62.1 (10.0)	65.9 (10.5)	58.4 (7.9)	<.001	0.82
SRS SR Total Score[c,d]	17.5 (9.82)	20.1 (10.6)	15.2 (8.5)	.002	0.52
AADIS: Frequency–Alcohol[e]	2 [0, 3]	2 [0, 3]	2 [0, 3]	.155	0.14[f]
AADIS: Frequency–Marijuana[e,f]	1 [0, 3]	1 [0, 5]	1 [0, 3]	.19	0.21[f]

Statistical test results shown are for comparison of the PSS and non-PSS groups. YSR/ASR syndrome scale scores are presented as mean T scores (SD). See Figures S1A–L for substance use frequency for each substance captured on the AADIS. Continuous variables are presented in mean (SD) format; number and percentage of participants endorsing the item are shown.

AADIS, Adolescent Alcohol and Drug Involvement Scale; ASR, Adult Self-Report; CIS SR, Columbia Impairment Scale Self-Report version; C-SSRS, Columbia-Suicide Severity Rating Scale; GF, Global Functioning Scale; NSSI, nonsuicidal self-injury; PQ-B, Prodromal Questionnaire – Brief; PSS, psychosis spectrum symptom; SOPS, Scale of Prodromal Symptoms; SIQ-Jr, Suicidal Ideation Questionnaire–Junior; SRS SR, Social Responsiveness Scale Self-Report version; WHODAS SR, World Health Organization Disability Assessment Schedule Self-Report version; YSR, Youth Self-Report.

[a]These effect sizes are Cohen's *d*, based on mean differences, and are presented here for descriptive purposes.

[b]Binary variables.

[c]The Social Problems Syndrome Scale is only part of the YSR (*n* = 187 youth participants).

[d]SRS SR (*n* = 179 youth participants ≥ 18 years old).

[e]Denotes median [Q1, Q3], with Mann-Whitney *U* tests used to evaluate group differences.

[f]AADIS Frequency—marijuana includes marijuana, hashish, poppers (marijuana with tobacco), K2, and spice.

In these early findings from the TAY Cohort Study, there are also some limitations. In these initial analyses, we have utilized the PRIME Screen–Revised Extreme Agreement Index for demarcating the presence of PSSs, which represents one of several approaches for indicating clinically significant PSSs. We did not include other indices of PSSs including severity based on the Prodromal Questionnaire–Brief, the Scale of Prodromal Symptoms negative/disorganized symptoms, or age-deviant *z* scores on the PRIME Screen–Revised, as was done in the PNC study (9), which may have identified additional individuals meeting PSS criteria. However, these approaches will be utilized in the TAY Cohort Study in analyses with the full sample. Across the longitudinal aims of the TAY Cohort Study, there is also the risk of participant attrition, which is common with such cohort studies. We have embedded engagement with youths and caregivers to guide study design, scheduling of assessments, and optimization of the package of assessments to enhance participant experience and minimize potential loss of participants to follow-up. In addition, a unique feature of this developmental cohort study is the linkage to health administrative data. This provides valuable information related to longitudinal patterns of health service use and outcomes, for both retained participant and those who may be lost to follow-up from the primary data collection of this study, and provides an opportunity to measure diagnoses that may develop, medications that may be prescribed, and cost to the system. This will enable comparisons of whether specific subgroups of participants are lost to follow-up and their relative representativeness within the full sample.

We anticipate that the TAY Cohort Study will be uniquely valuable and highly complementary to community-based studies (e.g., PNC and ABCD Study) in that joint analyses of population cohort data with ours can enable tests of continuity versus discreteness of several behavioral readouts. Collecting

diverse and comprehensive information provides the opportunity to discover 1) whether there are detectable and relatively homogeneous subgroups of mentally ill youths within the population that are not adequately described by existing diagnoses; 2) which behavioral and socioenvironmental factors are most important in determining subgroup membership; and 3) whether subgroup membership holds clinically important prognostic or treatment-relevant information as it pertains to psychosis risk and prevention, respectively. Recent work has shown that such subgroups may exist and that membership in them may explain prognostic differences in bipolar disorder (53) or treatment response in schizophrenia (54).

Through modeling of the developmental pathways of youths with mental illness, the identification of psychosis risk trajectories, and associated health service utilization profiles, the longitudinal findings of the TAY Cohort Study can help differentiate subgroups of individuals. For example, PSSs may mark more severe versions of mental or neurodevelopmental disorders in some individuals (e.g., in youths with depression or ASD), who are also higher users of health services, and have poorer functioning. In other individuals, PSSs may be related to higher risk for emergence of a primary psychotic disorder, which has its own set of lifelong consequences. In others, PSSs may resolve. The conceptualization of youths with mental illness as a high-risk group presents new questions for psychosis prevention: For example, is it possible that effective treatment of antecedent mental health conditions might in and of itself act as a prevention mechanism for psychotic disorders? Given the adverse consequences of PSSs, could interventions moderate either their worsening or their impact on functioning? Future clinical trials with this cohort may be uniquely positioned to address these crucial questions.

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Establishing a TAY Cohort Study repository that will serve as a platform for data sharing (across the study team and with qualified researchers external to the study team and for comparison with findings from harmonized datasets) is critical to the success of this initiative. In support of open science, the TAY Cohort Study will utilize the data governance model established by the CAMH BrainHealth Databank, detailing policies, procedures, and processes for gaining and providing secure access to deidentified TAY Cohort Study data. In keeping with Canadian Ethical Standards, only data from participants who explicitly consent to sharing data for future secondary re-use will be included in data releases. Three data releases are planned: a baseline cross-sectional release, a release following completion of the 3-year longitudinal time point, and a final 5-year longitudinal release. Each release will be timed with the publication of primary research papers from the TAY Cohort Study Team. Released data will include summary scores, item-level data, and associated metadata and code. Before each data release, a risk of re-identification analysis will be conducted that includes an assessment for the uniqueness among indirect identifiers of the participants. The Brain Health Databank Data Steward may alter the initial dataset to mitigate the risk of re-identification.

The Brain Health Databank serves as the data repository for CAMH and is currently nearing approval by the CAMH Research Ethics Board. External researchers will use the web-based cohort finder to facilitate the completion of the data access request form. All researchers accessing the Brain Health Databank must agree to the Data Use Agreement terms, which detail how data would be cited and acknowledged. The Data Use Agreement also forbids "re-identification"; researchers cannot attempt to reveal the identity of any individual using the data provided. The data access requests reviewed and approved by a Data Access Committee will be available for download via the Brain Health Databank. Data will be available for download via the Brain Health Databank portal. Researchers will need to renew data access annually.

Limited data for a smaller sample size were presented in poster form at the 2023 Annual Congress of the Schizophrenia International Research Society, May 11–15, Toronto, Ontario, Canada (55).

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ARTICLE INFORMATION

From the Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto, Ontario, Canada (KC, GF, SHA, DBC, BIG, LDH, NK, LCQ, MR, ALW, BFA, MA, DM, MJ, MF, JK-YW, RK, EWD, DF, JDH, M-CL, YSN, WT, WW, MB, MOH, SK, PK, RDL, AP, PS); the Department of Psychiatry, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada (KC, GF, SHA, DBC, BIG, LDH, NK, LCQ, MR, BFA, MA, EWD, DF, JDH, YSN, WT, MB, MOH, SK, PK, RDL, PS, ANV); the Department of Physiology, University of Toronto, Toronto, Ontario, Canada (ALW); the Hospital for Sick Children, Neurosciences and Mental Health, Toronto, Ontario, Canada (ALW, PS); the Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom (MCL); the National Taiwan University Hospital and College of Medicine, Taiwan (MCL); and the Department of Psychology, University of Guelph, Guelph, Ontario, Canada (SPL).

The TAY CAMH Cohort Study Team: Madison Aitken (1,2), Stephanie H. Ameis (1,2), Brendan F. Andrade (1,2), Marco Battaglia (1,2), Isabelle Boileau (1,2), Kristin Cleverley (1,2), Darren B. Courtney (1,2), Andreea O. Diaconescu (1,2), Erin W. Dickie (1,2), Daniel Felsky (1,2), George Foussias (1,2), Benjamin I. Goldstein (1,2), Vanessa Gonçalves (1,2), John D. Griffiths (1,2), John D. Haltigan (1,2), Hayley Hamilton (1,2), Lisa D. Hawke (1,2), Sean Hill (1,2), Muhammad Omair Husain (1,2), Melanie Jani (1), Sean A. Kidd (1,2), Nicole Kozloff (1,2), Paul Kurdyak (1,2), Meng-Chuan Lai (1,3,4), Stephen P. Lewis (5), Robert D. Levitan (1,2), Hsiang-Yuan Lin (1,2), Yona Lunsky (1,2), Akshay Mohan (1,2), Yuliya S. Nikolova (1,2), Sam Osman (1), Shannon Pascoe (1), Alexia Polillo (1), Connie Putterman (1), Martin Rotenberg (1,2), Dafna Sara Rubin-Kahana (1,2), Lena C. Quilty (1,2), Harijah Sivakumar (1), Peter Szatmari (1,2,6), Wanda Tempelaar (1,2), Neil Vasdev (1,2), Wei Wang (1), Anne L. Wheeler (1,6,7), Anna I.R. van der Miesen (1), Erica L. Vieira (1,2), and Aristotle N. Voineskos (1,2).

(1) Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto, Ontario, Canada; (2) Department of Psychiatry, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; (3) Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom; (4) National Taiwan University Hospital and College of Medicine, Taiwan; (5) Department of Psychology, University of Guelph, Guelph, Ontario, Canada; (6) Hospital for Sick Children, Neurosciences and Mental Health, Toronto, Ontario, Canada; (7) Department of Physiology, University of Toronto, Toronto, Ontario, Canada.

KC and GF contributed equally to this work as joint first authors.

Address correspondence to Aristotle Voineskos, M.D., Ph.D., at Aristotle.Voineskos@camh.ca.

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